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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/418,176	10/13/1999	GOUTAM DAS	1103326-0206	8505

7470 7590 11/17/2003

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PATENT DEPARTMENT
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EXAMINER	
RAMIREZ, DELIA M	
ART UNIT	**PAPER NUMBER**
1652	

DATE MAILED: 11/17/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/418,176	DAS, GOUTAM	
	Examiner	Art Unit	
	Delia M. Ramirez	1652	

-- Th MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 August 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,14 and 15* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,10-12 and 14* is/are rejected.

7)☒ Claim(s) *9 and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority und r 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Application

Claims 1-12 and 14-15 are pending.

Applicant's amendment of claims 1 and 4, as filed on 8/21/2003 is acknowledged.

Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

Claim Rejections - 35 USC § 112, First Paragraph

1. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

2. Claims 9 and 15 were rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

3. In view of a statement by Applicant's attorney of record over his signature and registration number, indicating that the specific vector/strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, this rejection is hereby withdrawn.

Claim Rejections - 35 USC § 103

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. Claims 1-2, 4-8, 10-12, 14 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (U.S. Patent No. 5,200,183, 1993; cited in previous Office Actions) in view of Yamada et al. (Biochimica et Biophysica Acta 1206: 279-285, 1994).

6. Claim 3 remains rejected under 35 U.S.C. 103(a) as being unpatentable over Tang et al. (U.S. Patent No. 5,200,183, 1993; cited in previous Office Actions) in view of Yamada et al. (Biochimica et Biophysica Acta 1206: 279-285, 1994) as applied to claims 1-2, 4-8, 10-12, 14 above, and further in view of Martinez et al. (EP 0-438-200 A1, 1991; cited in previous Office Actions).

7. These rejections have been discussed at length in Paper No. 15, mailed on 2/21/2003.

8. Applicants argue that at the very most Applicant's invention would be obvious to try but not obvious to do. Applicants submit that the courts have established that the standard of nonobviousness is not obvious to try but obvious to do. Applicants also submit that the Examiner has dismissed the Ratner reference ignoring various teachings from this reference and has instead pointed out the amount of time elapsing between the publication date of the Ratner reference and that of the filing of the instant application to imply that the knowledge obtained in the intervening years contravenes the teachings of Ratner. It is Applicant's opinion that one or two instances of success do not overcome the overwhelming battery of evidence teaching the complexities and uncertainties attendant upon devising an invention such as that of the instant application. According to Applicants, the amount of time elapsing between the Ratner publication and the filing of the instant application are indicative of the lack of motivation to make the instant application. Furthermore, Applicants submit that according to Ratner, (1) optimal expression of a given protein depends upon a number of considerations, (2) there is uncertainty as to whether products expressed in yeast or P. pastoris are appropriately glycosylated, (3) evaluation of an expression system must be done on a case-by-case basis and that each system is protein specific, and (4) Genzyme was reluctant to consider a license in regard to the expression of human t-PA in P. pastoris due to questions in regard to its biological activity. Applicants argue that glycosylation plays an important role in the proper folding of proteins and that in the case of BSSL, which is heavily glycosylated, would not have predicted that expression in P. pastoris would render an appropriately glycosylated enzymatically active protein. In addition, Applicants submit that until the present invention, one could have not been

certain that BSSL expressed in P. pastoris would not be subjected to endogenous cellular proteolytic degradation.

9. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the obviousness rejection. While the Examiner acknowledges that (1) the standard of nonobviousness is not obvious to try but obvious to do, (2) complexities and uncertainties in the production of recombinant proteins, (3) the teachings of Ratner as indicated above, (4) glycosylation plays an important role in the proper folding of proteins, and (5) a recombinant protein can be subjected to proteolytic degradation by the host cell, one of skill in the art would not only have the motivation to combine the teachings of Tang et al. and Yamada et al., as indicated in Paper No. 15, but would also have a reasonable expectation of success at combining such teachings and obtain the claimed DNA construct. In the obviousness analysis, one is not required to show absolute certainty of success but rather a reasonable expectation of success. In the instant case, the Examiner has provided the teachings of Yamada et al. to show that one of skill in the art would have a reasonable expectation of success at making a vector which can be used in P. pastoris to express a human protein. In addition, Applicant's own specification discloses prior art examples of P. pastoris being used to express human proteins. See page 4, lines 1-5. Therefore, while it is agreed that there is not absolute assurance that BSSL expressed in P. pastoris would be successful, in view of the many reports of successful expression of recombinant proteins in P. pastoris as indicated by Applicants and the Examiner, it is unclear as to how one could not reasonably expect successful expression of BSSL in P. pastoris. The Examiner is not neglecting the teachings of Ratner and agrees that in recombinant protein expression many factors have to be considered, such as glycosylation or proteolysis, and in many instances, it is protein specific. However, in the instant case, U.S. Patent No. 5827638 (same assignee as that of the instant application) shows that active BSSL can be produced even in E. coli (column 14, lines 10-35), which is a prokaryotic host cell incapable of glycosylation. Therefore, it is unclear as to how it would be unexpected that BSSL recombinantly produced in P. pastoris would be enzymatically active,

since active BSSL has been expressed in a prokaryotic host cell. In regard to proteolytic degradation, it is noted that degradation of recombinant proteins by host's proteases is a problem which can be encountered in any expression system since all host cells produce proteases. One of skill in the art would expect some proteolytic degradation of the desired protein in P. pastoris and still would have a reasonable expectation of being able to recombinantly produce BSSL since it is not expected that all of the produced BSSL would be proteolytically degraded. In regard to arguments that the amount of time elapsing between the Ratner publication and the filing of the instant application are indicative of the lack of motivation to make the instant application, this is not found convincing since the criteria for determining obviousness in Graham vs. John Deere does not include a time limit after which an invention is non-obvious. Thus, for the reasons set forth above and those of record, the invention as a whole would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made.

Double Patenting

10. Claims 1-2, 4-8, 10-12, 14 remains rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5827683 (common assignee ASTRA AKTIEBOLAG) in view of Yamada et al. (Biochimica et Biophysica Acta 1206: 279-285, 1994).

11. Claim 3 remains rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of U.S. Patent No. 5827683 in view of Yamada et al. (Biochimica et Biophysica Acta 1206: 279-285, 1994) as applied to claims 1-2, 4-8, 10-12, 14 and further in view of Martinez et al. (EP 0-438-200 A1, 1991; cited in previous Office Actions).

12. These rejections have been discussed at length in Paper No. 15, mailed on 2/21/2003.

13. Applicants argue that for the same reasons set forth in regard to the obviousness rejections, the double patenting rejections should be withdrawn.

14. Applicant's arguments in regard to the obviousness rejections have been addressed above. Since they are not deemed persuasive to overcome the obviousness rejections previously applied and no terminal disclaimer has been filed, the double patenting rejections are maintained for the reasons of record.

Allowable Subject Matter

15. Claims 9 and 15 are allowable over the prior art of record but are objected to since they depend upon rejected claims.

Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

17. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 308-4556. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (703) 306-0288. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (703) 308-3804. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Delia M. Ramirez, Ph.D.
Patent Examiner
Art Unit 1652

DR
October 23, 2003